

DRUG NAME: Ibritumomab**SYNONYM(S):** ibritumomab tiuxetan, ⁹⁰Y-ibritumomab tiuxetan**COMMON TRADE NAME(S):** ZEVALIN®**CLASSIFICATION:** radiopharmaceutical, cytotoxic¹

Special pediatric considerations are noted when applicable, otherwise adult provisions apply.

MECHANISM OF ACTION:

Ibritumomab is a murine IgG1 monoclonal antibody which is covalently bound to the chelating agent tiuxetan. It reacts specifically with the CD20 antigen, which is present in 93% of patients with B-cell non-Hodgkin's lymphoma. The cytotoxic activity of ibritumomab is provided by further chelation with the radioactive yttrium-90 (⁹⁰Y). It does not appear to be cell cycle phase specific.²

USES:**Primary uses:**

* Lymphoma, non-Hodgkin's²

*Health Canada approved indication

Other uses:**SPECIAL PRECAUTIONS:**

Contraindicated in patients with known hypersensitivity to any component of the treatment regimen, including yttrium chloride and rituximab.²

Caution:

- severe and prolonged cytopenias may occur; patients particularly at risk include:
 - those who have been treated with fludarabine, especially if <4 months ago
 - those with ≥25% marrow involvement and/or impaired bone marrow reserve
 - those with thrombocytopenia at baseline
- severe mucocutaneous skin reactions may occur, and may be fatal
- absolute maximum allowable dose of ⁹⁰Y-ibritumomab is 32 mCi (1184 MBq)
- intended as a single course of treatment; safety of multiple courses of ibritumomab has not been established
- should be received, used, and administered only by professionals trained in the safe handling of radionuclides
- patients who have received murine proteins should be screened for human anti-mouse antibodies (HAMA), and may be at increased risk of hypersensitivity reactions
- rituximab is an essential component of ibritumomab-based regimens, and rituximab precautions apply; refer to the [Rituximab Monograph](#) for more information, especially concerning infusion reactions

SIDE EFFECTS:

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials, and/or determined to be clinically important. When placebo-controlled trials are available, adverse events are included if the incidence is $\geq 5\%$ higher in the treatment group.

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in <i>bold, italics</i>	
Side effects and incidence are based on a regimen containing radiolabelled ibritumomab unless specified	
allergy/immunology	angioedema (5%, severe <1%)
	infusion reactions; severe, fatal in some cases; refer to Rituximab Monograph
blood/bone marrow/ febrile neutropenia	anemia (61%, severe 17%)
	<i>neutropenia</i> (77%; severe 57%, increasing to 74% in patients with baseline thrombocytopenia); nadir 7-9 weeks, duration 22-35 days
	<i>thrombocytopenia</i> (95%, severe 61%, increasing to 78% in patients with baseline thrombocytopenia); nadir 7-9 weeks, duration 22-35 days
constitutional symptoms	asthenia (43%, severe 3%)
	chills (24%, severe <1%)
	fever (17%, severe 1%)
dermatology/skin	<i>extravasation hazard: none</i>
gastrointestinal	<i>emetogenic potential: low²</i>
	abdominal pain (16%)
	nausea (31%, severe 1%)
	vomiting (12%, severe 0%)
infection	infection (29%, severe 5%); fatalities have occurred
musculoskeletal	weakness (43%)
pain	headache (12%, severe 1%)
	pain (13%, severe 1%)
pulmonary	dyspnea (14%, severe 2%)

Adapted from standard reference² unless specified otherwise.

SUPPLY AND STORAGE:

Injection: Berlex supplies a kit containing the non-radioactive ingredients required for the preparation of ⁹⁰Y-ibritumomab: one vial containing 3.2 ibritumomab tiuxetan in 2 mL NS (1.6 mg/mL), one 50 mM sodium acetate vial, one formulation buffer vial, one empty reaction vial, and four identification labels. Nonmedicinal ingredients include: human serum albumin.²

SOLUTION PREPARATION AND COMPATIBILITY:

Ibritumomab should only be prepared by a qualified specialist in handling radiopharmaceuticals.

PARENTERAL ADMINISTRATION:

BCCA administration guideline noted in ***bold, italics***

Subcutaneous	no information found
Intramuscular	no information found
<i>Direct intravenous²</i>	<i>over 10 minutes</i>
Intermittent infusion	no information found
Continuous infusion	no information found
Intraperitoneal	no information found
Intrapleural	no information found
Intrathecal	no information found
Intra-arterial	no information found
Intravesical	no information found

DOSAGE GUIDELINES:

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response and concomitant therapy. Guidelines for dosing also include consideration of absolute neutrophil count (ANC). Dosage may be reduced, delayed or discontinued in patients with bone marrow depression due to cytotoxic/radiation therapy or with other toxicities.

Adults:***Intravenous²:***

BCCA usual dose noted in ***bold, italics***
0.4 mCi/kg IV for one dose on day 8 (total dose 0.4 mCi/kg)
Absolute maximum dose 32 mCi (1,184 MBq), regardless of patient weight.

REFERENCES:

1. National Institute for Occupational Safety and Health (NIOSH). Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Healthcare Settings. Cincinnati, OH; September 2004.
2. Berlex Canada. ZEVALIN® product monograph. Pointe-Claire, Quebec; 10 May 2005.